APOLIPOPROTEIN B, A HIDDEN RISK FACTOR AMONG PATIENTS REQUIRING INVASIVE THERAPY FOR CORONARY ARTERY DISEASE

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Recent studies in our laboratory have demonstrated the beneficial effects of lipid altering therapy in patients with coronary artery disease (CAD) and elevated apolipoprotein B (apoB). To determine the prevalence of elevated apoB and other lipid abnormalities among CAD patients, we performed a detailed lipoprotein analysis on two unselected populations with clinically limiting CAD: 222 patients undergoing bypass grafting (CABG) and 166 patients undergoing coronary angioplasty (PTCA). Plasma samples were obtained at cardiac catheterization. Lipid Research Clinic methods and population data were used to determine and to rank low and high density lipoprotein cholesterol (LDL_C, HDL_C), total plasma apoB, and triglycerides (TG). Abnormal was defined as ≥90th percentile for age and sex (≤10th percentile for HDL_C). For apoB, this is ≥130 mg/dl for a 48 year old male.

Results:

Group	Age	N	Percent of subgroup with abnormal levels of: ApoB	LDL_C	HDL_C	TG	ApoB only
CABG	<50	43	56	26†††*	23**	19*	21
	>50	179	40	12*	35**	16*	13
PTCA	<50	49	55††	22†*	22*	24*	14
	>50	117	35	6*	13*	15*	21

χ^2 statistical comparison: Versus age >50: †p≤.001; ††p≤.02; ††† p≤.05
Versus apoB (all ages): * p≤.001; ** p≤.02

CONCLUSIONS: 1) ApoB elevation is significantly more common than LDL_C, HDL_C or TG abnormalities, particularly among younger patients; 2) 54% of all patients undergoing PTCA and 65% of those undergoing CABG have at least one lipid abnormality; and 3) ApoB measurement appears indicated, since it could guide therapy in 15% of all CABG patients, and 19% of PTCA patients, who have only apoB elevation, which is "hidden" from routine lipid screening.

QUANTIFICATION OF RATE OF CORONARY ARTERY DISEASE PROGRESSION BY A NEW METHOD OF ANGIOGRAPHIC ANALYSIS.

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Little is known about the rates and variability of atherostenosis progression in pt with evidence of coronary artery disease at baseline angiography. In order to assess the rate and variability of progression, we used a simplified quantitative method of analysis in studying single angiograms (A) in 54 pt and paired A in 29 pt. All discrete lesions were identified by consensus of 2 observers, then traced and digitized to determine lumen diameter (LD), and summed to give total LD; the differences in LD for paired A were summed to give total stenosis change (TSC). Results: Correlation of LD measured by our method and with the Brown method was excellent (R=0.99, N=54). Interobserver (R=0.98, N=29) and intraobserver (R=0.99, N=54) studies also showed a high correlation. Shortterm TSC (assessed in 9 pt with A paired at <1 wk) was negligible (0.03±0.38 mm). (Lesions undergoing coronary angioplasty or bypass surgery were excluded.) Longterm progression was then assessed in 20 pts. (A were paired at a mean of 2.1 yr; range, 0.6 to 4.3 yr). Longterm total LD (4.1±2.5 mm) differed significantly from baseline total LD (6.0±3.0 mm; p<0.001), and TSC (2.0±1.3 mm) in longterm pt differed significantly from TSC in shortterm (<1 wk) pt (p<0.001). These results show that true coronary disease progression occurring over 1 to 4 yrs can be distinguished from intraobserver, interobserver, and interstudy variability using a simplified method, and provide approximate rates and variability of progression. These results will be useful for power calculations in therapeutic trials aimed at reducing progression. Further prospective studies using this method appear indicated.

PLASMA HDL SUBFRACTIONS AND APOPROTEIN A-I AS PREDICTORS OF ANGIOGRAPHIC CORONARY DISEASE IN NORMOLIPIDEMIC MEN.

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Many patients with coronary artery disease (CAD) have desirable levels of total cholesterol (TC) and triglyceride (TG). We have previously demonstrated that HDL-C, HDL_3-C, and apoprotein (apo) A-I are inversely correlated with the presence of CAD. To determine their predictive values, these analytes were assayed in male patients undergoing elective coronary arteriography. All had TC and TG levels <225mg/dl, and no history of hypertension or diabetes. Patients were categorized as either free of significant CAD (<20% obstruction in a coronary artery or branch, n=26) or with clinically relevant CAD (≥70% obstruction, n=61). The Student t test demonstrated the following to be lower in the CAD group: HDL_3-C(38±1mg/dl vs 32±1mg/dl, p<.0001), HDL-C(44±2mg/dl vs 37±1mg/dl, p<.01) and apo A-I (109±5 mg/dl vs 99±2mg/dl, p<.03). Linear discriminant analysis identified HDL_3-C and age to be the most important variables for predicting the presence or absence of CAD. Patients can be classified as having either normal coronaries or clinical CAD using the following equations derived from linear discriminant analyses:

L_{Normal}=-31.00+1.002(HDL_3-C)+0.43364(age)
L_{CAD}=-29.89+0.82303(HDL_3-C)+0.52144(age)

The larger of the two values obtained after incorporating a patients' age and HDL_3-C value into both equations, determines if the patient falls into the normal or CAD group. The probability of correctly classifying a patient is 69% for the normal group and 80% for the CAD group. This sensitivity and specificity makes HDL_3-C potentially useful in screening normolipidemic patients with chest pain for consideration of coronary arteriography to confirm the presence of CAD.

Is Routine Automated Quantitative Analysis of Coronary Arteriography Feasible? Evaluation of Operator-Dependent Variables Inherent to the Technique

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Although automated quantitative arteriography (QA) has been shown to reduce variability and increase precision in measurement of stenoses, controversy exists regarding the suitability of QA for routine analysis of coronary arteriograms. Therefore, QA was prospectively performed by 4 independent observers in 35 consecutive patients undergoing coronary arteriography for clinical indications. In 25 patients, a significant stenosis of ≥50% was identified by at least one observer (130 sites). Only 69/130 (53%) of these lesions were graded as significant (≥50%) by 3 of 4 observers, and only 38/130 (29%) were graded significant by all 4 observers. In the subgroup of unanimously identified lesions, all 4 observers selected the same projection for QA in 23% of cases and the same image frame in 2.1% of cases. For this group, all observers applied automated QA to all lesions utilizing a previously validated border detection program. Eighteen of the 38 lesions were not suitable for automated arterial border detection because of bifurcation or major sidebranch, vessel overlap and/or low image contrast. In these situations, a manual QA method was utilized. For the group of unanimously selected lesions suitable for automated border detection, interobserver variability for QA of single image frames was very low, 4.8% when a frame was preselected. However, variability increased significantly to 7.2%, (p<.01) when observers were permitted to select the projection and frame for analysis. For the group of lesions requiring manual QA, higher interobserver variability was seen (9.8%). These data indicate that several operator-dependent variables in identification and selection of projection and frame to be measured can substantially influence the reproducibility of automated QA. Additional sources of operator-dependent variability include selection of stenosis and reference vessel locations. For lesions unanimously identified as ≥50% stenosis, automated QA is possible for only 53%. Automated QA does not appear to be suitable for routine clinical application at the present time.